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| 10/626,502 | 07/23/2003 | Kyoichi Sumida | 14633.1US01 | 1967 |

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Hamre, Schumann, Mueller & Larson, P.C.
P.O. Box 2902-0902
Minneapolis, MN 55402

| EXAMINER | |
|---|---|
| FETTEROLF, BRANDON J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 11/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/626,502 | SUMIDA ET AL. | |
| | Examiner | Art Unit | |
| | Brandon J. Fetterolf, PhD | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 9-15* is/are rejected.

7)☒ Claim(s) *8 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Application Status*

Claims 1-16 are currently pending and under consideration

### *Priority*

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Japan on 06/05/2001. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter.

### *Information Disclosure Statement*

The Information Disclosure Statement filed on 03/04/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

### *Specification*

The disclosure is objected to because of the following informalities: The specification makes several references to a CRP concentration and refers to the concentration as mg/dL, see for example on page 4, lines 25-26 and page 29, line 1. However, the Examiner believes that concentration should be referred to as mg/mL.

Appropriate correction and/or clarification is required.

### *Claim Objections*

Claims 1-16 are objected to because of the following informalities: While claims 1-10 appear to be directed to a method, the recitation in the claims of "An immunoassay" is confusing. For

clarification purposes, it may be less confusing if the claims were to recite "An immunoassay method". Furthermore, claims 11-16 appear to be directed to kit, e.g. a product. However, the recitation of active steps, e.g., combining a reagent of a copolymer and a reagent containing an antibody ..., is confusion. For clarification purposes, it may be less confusing if the active step, e.g., combining, was removed such that the claims would recite ... A kit of reagent for immunoassay of a prostate specific antigen comprising a reagent containing a copolymer.... Appropriate correction and/or clarification is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the instant case, Claim 13 recites "[T]he kit according to claim 12, wherein the antibody to a prostate-specific antigen or the prostate-specific antigen is an antibody supported on a carrier." However, Claim 12 already sets forth that the antibody or prostate-specific antigen are supported on a carrier and further, it is unclear how a prostate specific antigen can be an antibody. Thus, it is unclear what Applicant's are attempting to claim. For examination purposes, claim 13 will be interpreted as being identical to claim 12 and as such, claim 14 will depend from claim 12.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7 and 9-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eda et al. (U.S. 6248,597, 2001) in combination with Shigenobu et al. (WO 02/018953, 2002).

(Note: All references to the Shigenobou et al. WO publication will be directed to the English translated EP patent application (EP 1314982 A1, 2003))

Eda et al. teach an agglutination immunoassay of an antigenic analyte comprising performing an antigen-antibody reaction in the presence of a microparticle, wherein the microparticle includes polymeric materials as well as copolymers thereof (column 4, line 67 to column 5, line 5 and column 7, lines 12-19). With regards to the antigenic analyte, the patent teaches (column 5, line 47) that the antigenic analyte may be a tumor marker such as prostate specific antigen (PSA).

Eda et al. does not explicitly teach that the polymer and/or copolymer is represented by the monomer presented in formula [2] and a monomer selected from the group consisting of acrylic acid or acrylate ester, or methacrylic acid or methacrylate ester or styrene. Further, Eda et al. does explicitly teach a kit comprising a copolymer obtained by polymerizing a monomer of formula [2] with a second monomer and a prostate specific antibody.

Shigenobu et al. teach a method of improving the reproducibility of an agglutination immunoassay comprising allowing an antigenic substance in a sample to bind to insoluble carrier particles and allowing an antibody or an antibody complex which reacts specifically to the antigenic substance to bind to the antigenic substance in the presence of a polymer (page 2, line 25 and lines 43+). With regards to the insoluble carrier, Shigenobu et al. teach (page 4, lines 24-39) that the insoluble carrier may be latex. With regards to the polymer, the reference teaches (page 5, lines 4-29) that the polymer includes either a polymer having a monomer unit derived from the patently disclosed monomer represented by the general formula [2], wherein the monomer represented by formula [2] is that of 2-methacryloyloxethyl phosphorylcholine (see Sakaki et al. J. Biomedical Materials Research 1999; 47: 523-528 for structure) or a copolymer obtained by polymerizing the monomer represented by 2-methacryloyloxethyl phosphorylcholine with a "second" monomer selected from the group consisting of (meth)acrylates such as acrylate ester, a methacrylate ester, butyl methacrylate or styrene derivatives. Shigenobu et al. further teach (page 5, lines 50-58) that the ratio of the monomer unit derived from 2-methacryloyloxethyl phosphorylcholine in the copolymer is from 1% to 100% and the total polymer molecular weight is 100 to 1,000,000. In addition to the agglutination assay described above, the WO document teaches (page 8, lines 36-47)

a reagent kit for an immunoassay comprising combining a reagent containing a copolymer obtained by polymerizing 2-methacryloyloxethyl phosphorylcholine with a monomer as described above, an antibody that binds to the antigen in the sample, and an insoluble carrier protein such as latex, wherein the carrier protein supports the antigen.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Eda et al. and Shigenobu et al because each of the immunoassays have been individually taught in the prior art to be successful at the detection of antigens. Further, one would have been motivated to do so because as taught by Shigenobu et al., it is difficult to have a reaction in an agglutination immunoassay, which has good reproducibility due to the non-uniformity of agglutination in an agglutination reaction of the insoluble carrier particles with antigens or antibodies (page 2, lines 19-20). Thus, one of ordinary skill in the art would have a reasonable expectation that by combining the agglutination assay for PSA as taught by Eda et al. with the polymeric material used in the agglutination immunoassay as taught by Shigenobu et al., one would successfully achieve a highly reproducible agglutination immunoassay for prostate specific antigen.

Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eda et al. (U.S. 6248,597, 2001) in combination with Shigenobu et al. (WO 02/018953, 2002) in further view of Sakaki et al. (JP 2000-093169, 2000, Abstract).

Eda et al. and Shigenobu et al. teach, as described above for claims 1-4, 7 and 9-15, a highly reproducible immunoassay of a prostate specific antigen comprising performing an antigen-antibody reaction in the presence of either a polymer having a monomer unit derived from 2-methacryloyloxethyl phosphorylcholine or a copolymer obtained by polymerizing the monomer unit derived from 2-methacryloyloxethyl phosphorylcholine with a "second" monomer. With regards to the "second" monomer, Shigenobu et al. teaches that the "second" monomer includes, but is not limited to styrenes or methacrylates such as acrylate ester, a methacrylate ester, butyl methacrylate or styrene derivatives. Eda et al. and Shigenobu et al. further teach a reagent kit for an immunoassay comprising combining a reagent containing a copolymer obtained by polymerizing 2-methacryloyloxethyl phosphorylcholine with a monomer as described above, an antibody that binds

to the antigen in the sample, and an insoluble carrier protein such as latex, wherein the carrier protein supports the antigen.

Eda et al. and Shigenobu et al. do not explicitly teach that the "second" monomer is an N-alkyl methacrylamide or N-aralkyl methacrylamide.

Sakaki et al. teach a polymer/enzyme conjugate and polymer/enzyme/antibody conjugate useful for an enzyme immunoassay. Specifically, the JP Patent abstract teaches that the polymer was obtained by polymerizing a monomer possessing a phosphorylcholin-analog group (e.g. 2-methacryloyloxyethyl phosphorylcholine) and a monomer selected from methacrylate or 2-aminoethyl (meth)acrylate (abs).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the second "monomer" as taught by Shigenobu et al. with a "second" monomer such as an N-alklyl or aralkyl methaacrylamide in view of the teachings of Sakaki et al . One would have been motivated to do so because as taught by Sakaki et al., the polymer used in the immunoassay was obtained by polymerizing a monomer possessing a phosphorylcholin-analog group (e.g. 2-methacryloyloxyethyl phosphorylcholine) with a monomer such as 2-aminoethyl (meth)acrylate (abs). Thus, one of ordinary skill in the art would have a reasonable expectation that by substituting 2-aminoethyl (meth)acrylate as taught by Sakaki et al. for the "second" monomer as taught by Shigenobu et al., one would achieve a reagent which can be used in an immunoassay.

Note: The prior art does not appear to teach or suggest the polymerization of 2-methacryloyloxyethyl phosphorylcholine with benzyl methacrylate. Nor does the prior art appear to suggest a motivation to combine. As such, claims 8 and 16 are objected to as being drawn to a rejected independent claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
10/31/05